8-1-2015

Current Medical Research: Summer/Fall 2014

Richard Fehring
Marquette University, richard.fehring@marquette.edu

Intercourse During Implantation May Lead to Early Pregnancy Loss

Theoretically, intercourse during the time of implantation of a human embryo could result in an early miscarriage due to uterine contractions. In order to test this theory, researchers conducted a study to determine whether intercourse around the time of implantation reduced fecundability, i.e., the probability of obtaining a positive pregnancy test (Steiner et al. 2014). This study was a secondary analysis of a data set that was obtained from women attempting to achieve pregnancy between the ages of 30 and 44, had no known fertility problem, and had been trying to achieve pregnancy 3 months or less. The women were obtained through advertisement (radio and television), the Internet, e-mail, and informational letters. All participants were asked to keep a daily diary of their menstrual cycle, including intercourse, use of luteinizing hormone (LH) testing, and observations of cervical mucus changes. This study included 564
women (or 76% of the total 743 women enrolled into the study) who completed at least one menstrual cycle of data.

The researchers utilized a calendar-based calculation to determine the estimated day of ovulation, i.e., 14 days before the following menses was the estimated day of ovulation and days 5–9 following the estimated day of ovulation were the estimated days of embryo implantation. For this study there was 1,332 menstrual cycles, but only 46 percent had 2 to 3 days of intercourse during the fertile window. They discovered that couples who had two or more days of intercourse during the estimated postovulation implantation window were close to 40 percent less likely to have a positive pregnancy test compared to those couples who did not have intercourse during the estimated implantation window (fecundability ratio = 0.59; 95% CI: 0.40–0.86). They also noted that the probability of a positive pregnancy test decreased as the frequency of days with intercourse increased during the estimated implantation window. Although the authors concluded that intercourse during the estimated implantation window may reduce the ability to achieve a pregnancy, they did not recommend any change of practice. They did recommend further research.

Comments: An obvious limitation of this study was use of a calendar formula to estimate the day of ovulation and the estimated days of probable implantation. However, a sub group of 156 participants did use an LH test to estimate fertility, and generated 226 menstrual cycles of data, and found (based on intercourse on days 6–10 after the LH surge) a 26 percent less likelihood to achieve a positive pregnancy test compared to couples who did not have intercourse during that time period. However, the decrease in pregnancy rates did not reach statistical significance among this subset of participants. I would also point out that the frequency of intercourse might have been under reported.

Source

Use of Focused Intercourse during Estimated Fertile Phase Found to Be No Better Than Frequent Random Intercourse on Time to Pregnancy and Fecundability

Research studies have established that there is a window of fertility during the menstrual cycle that includes the day of ovulation and the five preceding days. The six day fertile window is based on the biological knowledge that sperm can live for 3 to 5 days in a good (cervical mucus) environment and that the egg following ovulation lives only for 24 hours or less. Therefore, it makes sense that having intercourse during this fertile window would increase the chance of pregnancy. However, having frequent intercourse (i.e., two to three times a week) might work as well, since some of those frequent acts of intercourse would automatically land on a day of the fertile window. Researchers sought to determine whether use of a method of natural family planning to estimate the fertile window and target intercourse would increase the time to pregnancy and fecundity (Stanford, Smith, and Varner 2014).

The participants for this study were women with no known infertility problems, were between the age of 18 and 35 years, had a pregnancy within the past 8 years, not currently breastfeeding, not on any hormonal contraceptives, and have regular menstrual cycle lengths. Participants were sought through e-mail, web site, mailings, newspaper advertisement, and person to person contact. The researchers were able to screen 667 potential participants, but of these, 247 were eligible, and of these, 104 declined participation. The remaining 141 were randomized into a group that was taught the Creighton Model System (CrMS) of natural family planning (n = 69) and another group that was asked to have frequent intercourse at least two to three times per week (n = 71). The CrMS is a cervical mucus only method of natural family planning with a standardized mucus rating and follow-up system. Participants were paid to provide menstrual cycles of data. All participants were provided a blinded electronic hormonal monitor that estimated the fertile window based on urinary measures of estrogen and luteinizing hormone (LH).
Based on menstrual cycles in which couples intended to conceive, the fecundity was 31 percent in the control (i.e., the frequent intercourse group) and 36 percent in the CrMS group ($P = 0.32$). The time to pregnancy for those who conceived was 2.9 cycles in the control group and 3.5 in the CrMS group. The cumulative probabilities of pregnancy for those couples attempting to conceive were 51 and 63 percent (respectively for the control group and the CrMS group) by menstrual cycle 3, and 88 and 93 percent (respectively for the control group and the CrMS group) by cycle 7. The researchers concluded that the study found no impact of using the CrMS to focus intercourse during the fertile phase among couples with proven fertility compared with frequent intercourse. The authors suspected that the study might have been under powered statistically.

Comments: An instruction of the CrMS is to avoid intercourse during the first menstrual cycle of use and although the control group was also asked to avoid intercourse during the first menstrual cycle, it was obvious that more couples in the control group took advantage of the first cycle to achieve pregnancy. The authors felt that this instruction favored the control group and that the control group had a head start on achieving pregnancy. At the end of the first menstrual cycle, the control group fecundatility was 17 percent (12 out of 71) and the CrMS group was 4 percent (3 out of 69 ($P = 0.02$).

Source


Natural Family Planning Differentiates Women’s Perception of the Availability of Reproductive Health Services in Catholic Hospitals

Catholic hospitals and healthcare systems provide approximately 10 percent of the health care in the USA. Furthermore, in some smaller communities Catholic hospitals and Catholic healthcare systems are the only health services available. Previous research has
shown that Catholic hospitals that follow Catholic Church teachings prevent the use of “standard” (i.e. immoral) reproductive services and that obstetricians and gynecologists view Catholic health systems as preventing the availability of “full” (but often immoral) reproductive services. Researchers theorized that women patients of reproductive age would be surprised and disturbed if they understood that Catholic healthcare systems are limited in the provision of some types of women’s healthcare services (Guiahi, Sheeder, and Teal 2014). Therefore, these researchers set out to determine whether women of reproductive age would expect different reproductive services in a Catholic hospital compared to a secular or non-Catholic hospital. They hypothesized that there would be no difference in the types of reproductive services that potential women patients would expect in a Catholic hospital as opposed to a secular-based health system.

The researchers sought volunteer women participants of reproductive age from online lists and a web page advertisement. They randomized volunteer women participants who met their criteria into two groups. Both groups were provided a short vignette that described a new hospital in the Denver, Colorado area in which the respondent is receiving an annual exam. One of the hospitals was named Saint Ignatius and the other Metropolitan Hospital of Denver. There were 236 volunteer participants, and of these volunteers, 115 met the study criteria and were randomized into the “Catholic” hospital group and 121 in the secular hospital group. All participants were provided an online 11 item survey that asked whether they would be able to receive types of reproductive service at the designated hospital or not, including methods of contraception, emergency contraception, injectable hormones, IUD, sterilization, natural family planning (NFP), and termination of pregnancy for a fatal abnormality. There were no differences in the demographics of the two groups. Of interest, most respondents were single, white, and had no religion. The researchers found that there was no difference in expected availability of reproductive services other than NFP, which was expected to be offered at a higher rate for the Catholic hospital.

Comments: The obvious limitation of this study is that the respondents are self-selected and as such can be biased. Although the authors said that the participants represent the characteristics of reproductive age women in Denver, the women were sought through
the Internet and they were mostly white, single, and college graduates. The fact that most did not have a religion is also a trend in the USA but not the norm. Finally, although the women in the secular hospital group less frequently responded that they expected NFP services, there was a large majority of women (86%) in this group who expected to be able to receive NFP services in a secular hospital. I found it concerning that women in the survey do not understand that unethical practices would not be offered at a Catholic hospital.

Source


**Use of Ovulation Predictor Kits as Adjuncts When Using Fertility Awareness Methods (FAM’s): A Pilot Study**

Study reviewed by Mary Schneider, M.S.N., F.N.P.

The use of an inexpensive urinary luteinizing hormone (LH) predictor test that can be used in conjunction with other biological fertility indicators, such as cervical mucus (CM) observations, has the potential of clarifying fuzzy signs of fertility and even increasing the use of fertility appreciation methods (FAM) in developed countries. Leiva et al. (2014) conducted a pilot study to see how efficient inexpensive urinary LH test kits were compared to FAM that used CM and/or basal body temperature (BBT) in identifying the postovulatory phase of the cycle. The purpose of the study was to determine feasibility of using an inexpensive urinary LH test kit with other biological signs of fertility employed by the FAM of choice to assist in identifying the postovulation phase of the menstrual cycle. Once LH was detected the women were asked to continue testing until they had three consecutive days of negative results, at which time the postovulatory gold standard test; serum progesterone levels were drawn from each participant. If the progesterone level was greater
than 10 nmol/L women participants were determined to be in the luteal phase of the cycle.

This pilot study was a two arm crossover block design that enrolled 23 regular cycling Canadian women with a high school education or higher and between the ages of 20 and 48. Women currently using hormonal contraception or trying to become pregnant at the time of recruitment were excluded. Sensitivity of the test kits used detected LH at 20 mIU/ml, a threshold that has been shown to be most accurate and least likely to miss the LH surge (Ecochard et al. 2001).

Women were assigned into either the FAM with LH test kit group or FAM only and after one cycle groups were switched. This technique was chosen to expose each group to both methods in hopes of avoiding learner bias. They began daily urine LH testing from the sixth day of menses through three consecutive days post the last positive LH test. That is, once the woman had a positive LH test she continued to test up to three consecutive negative days after the last positive. Serum progesterone levels were drawn on the third consecutive negative day. Statistical analysis using a McNemar test was used to detect differences between the two arms. Serum progesterone levels provided the markers for the dichotomous variables of “yes” the woman was in the luteal phase or “no” she was not.

*Comments:* The authors did find a statistically significant difference between the two methods. The participants using the LH test kits with FAM correctly identified the postovulatory phase 100 percent of the time and when FAM alone was used the postovulatory phase was correctly identified 87 percent of the time. However, to include both FAM methods, i.e., the CM FAM and the CM plus temperature FAM together could potentially skew the results. Although, both FAMs used tertiary signs of fertility (cervical mucus and/or BBT) to identify the postovulatory phase, the addition of temperature may confound the results because it is an objective sign of fertility like the LH test kit. The authors stated that they chose women who were having some difficulty identifying the peak day. Thus they were using the rules of the FAM method of their choice. Because there are several FAMs that are CM only or CM plus BBT with different
rules of identifying the peak day, it would be helpful if the type of methods within these groups were identified and analyzed separately.

Home urinary monitoring for estrogen, LH, and progesterone to identify ovulation and the fertile and infertile phases of the menstrual cycle is an achievable goal. This pilot study is a model for future FAM/natural family planning (NFP) research and another tool for the NFP teacher to place in their toolbox when dealing with women and couples having difficulty with identifying the peak of fertility and the postovulatory infertile phase of the menstrual cycle.

**Sources**


**Continuous Temperature Monitoring Correlated with Ultrasound**

Daily monitoring of basal body temperature (BBT) is a useful but fuzzy indicator of fertility for women using that indicator for purposes of avoiding or achieving pregnancy. Use of BBT is of particular concern since the upward shift in body temperature is due to the rise in progesterone post ovulation, hence, the indication of fertility is too late to affect an act of intercourse that would lead to pregnancy. However, newer temperature measuring devices have recently been developed that offer continuous temperature measurement and are thought to be more accurate than a single temperature upon rising in the morning. Such a device called the DuoFertility measures continuous temperature and movement by having the woman wear a sensor as an axillary patch. Researchers recently conducted a study to determine the accuracy of the device by comparing the continuous measure of body temperature with serial ultrasound of the developing follicle, i.e., the
gold standard of detecting the day of ovulation (Rollason, Outtrim, and Mathur 2014).

The researchers obtained eight volunteer women, 18–44 years of age, who presented to their clinic for treatment of fertility and who tried to conceive for 12 months or more. These participants were asked to monitor three consecutive menstrual cycles with use of the continuous temperature monitor and with the use of a daily luteninizing hormone (LH) urine tests starting on day 8 of their menstrual cycle. When they had a positive LH test they then came to the clinic for transvaginal ultrasound to monitor the dominant follicle and to document the collapse of the follicle. The day of the collapsed follicle was used as the estimated day of ovulation. The participants provided 35 menstrual cycles but only 18 cycles had complete data and were useful for the purpose of the study.

The researchers found that in every cycle that ultrasound detected the day of ovulation the temperature monitor did so as well. The estimated day of ovulation by use of the DuoFertility was 100 percent plus or minus 1 day of the ultrasound detected day of ovulation. In 10 of the cycles the temperature monitor detected ovulation on the estimated day of ovulation and in 3 one day after. The researchers realized that as a pilot study it did not have an adequate number of participants nor an adequate number of menstrual cycles of data. However, they indicated that the continuous temperature measurement device might be beneficial for infertile women with regular cycles with infertility problems and is less invasive than ultrasound measures.

Comments: Many women with infertility have irregular cycles and, as the authors indicated, future studies to test the accuracy and usability of this temperature monitoring device will need to include more participants and participants with irregular cycles. Although continuous measure of body temperature would provide a more accurate measure of temperature it still would be susceptible to body temperature variability that makes use of BBT difficult, i.e., during stress, lack of sleep, exercise, alcohol, infections, etc. Furthermore, since the DuoFertility BBT shift in body temperature was either on the day of ovulation or the day after, those days most likely are already too late for achieving pregnancy.
Premenstrual Spotting Found to Be Predictive of Endometriosis among Women with Infertility

Endometriosis can be a debilitating disease affecting about 6–10 percent of reproductive age women and is associated with pelvic pain and infertility. Since endometriosis is a progressive disease, diagnosing and surgically treating it early is important, i.e., before it becomes deeply invasive and infiltrating. Although there is some association of endometriosis with pelvic pain, the most definitive diagnostic procedure is through visual laparoscopy. Although laparoscopy is a fairly safe procedure, there are surgical risks and discomfort. Non-surgical diagnostic indicators would be beneficial for early and non-invasive detection. One potential indicator of early endometriosis is premenstrual spotting, i.e., light menstrual bleeding before a frank menses. Therefore, researchers sought to determine whether premenstrual spotting (of 2 days or more) was predictive of endometriosis among sub-fertile women (Heitmann et al. 2014).

The participants for this study were selected from the records of all women who underwent laparoscopy for an infertility assessment – most of whom had pelvic pain – from March 2009 to March 2011 at a tertiary medical center. All participants completed a three page infertility assessment that included questions as to pelvic pain during menses and intercourse, and whether they had spotting before the normal menstrual flow. The researchers only included the symptom if the premenstrual bleeding was two days or more before the onset of menses. They were able to obtain records of 80 women who met their criteria, and of these, 32 reported premenstrual spotting of two days or more. Of the women who reported premenstrual spotting, 89 percent, or 34 of 38, were diagnosed with endometriosis as compared to only 11 of 42 (26%) in the group of women who did not experience premenstrual spotting ($P < 0.001$). They also found that, of the three menstrual symptoms of dysmenorrhea, dyspareunia, or premenstrual spotting, premenstrual spotting was the most predictive, i.e., 81 percent.
percent compared to 76 percent for dysmenorrhea, and 58 percent for dyspareunia. A stated limitation of the study was the retrospective design. However, they concluded that if this association of premenstrual spotting and endometriosis is validated in prospective studies that it could be used for the identification of women who would benefit most from laparoscopic evaluation and treatment.

Comments: I would also add that a prospective study that incorporates prospective charting of the menstrual cycle that includes natural biological markers of fertility and levels of menstrual bleeding, i.e., charting systems that are commonly found in natural family planning systems, would provide a more accurate assessment of premenstrual spotting. This study also reinforces the benefit of charting the menstrual cycle as a vital sign for women's health.

Source


Use of Electronic Fertility Monitoring versus Cervical Mucus Monitoring Results in Less Abstinence and More Frequent Coitus for Couples Using Natural Family Planning

Study reviewed by Kathleen M. Raviele, M.D., Ob/Gyn, F.A.C.O.G.

Despite modern methods of natural family planning (NFP) being readily available, there are few couples who use these safe and natural methods. Only 0.1 percent of women in the USA are using a method of NFP. Reasons for the lack of use may include prolonged abstinence, difficulty with observations, difficulty in learning the method, and unexpected pregnancies. There is a need for continued research efforts to develop safe, easy methods of NFP to assist couples in living out the teachings of the Catholic Church in the area of family planning.
Fehring and Schneider (2014) conducted an analysis of data from a 12-month prospective comparison study where couples were randomized into an online NFP method that included either the use of an electronic fertility monitor (EHFM) and a fertility algorithm for the beginning of the fertile window in one group and cervical mucus monitoring (CMM) and a fertility algorithm for the beginning of the fertile window in the other group. After 6 months of use, the fertility algorithm was adjusted for the earliest peak day seen either with the monitor or the mucus. The goal of the study was to compare the estimated time of fertility, and thus days of abstinence, between the two methods, as well as the frequency of intercourse between the two methods.

A total of 197 women were in the EHFM group and 160 women in the CMM group and they were observed over 1,663 menstrual cycles of data. The women were 18–42 years of age, with a cycle length of 21–42 days, and they were more than 3 months off hormonal contraceptives as well as more than 3 months past breastfeeding. There was no demographic difference between the two groups in age, parity, age of male partner, or BMI. They learned the method online and were instructed in how to make the mucus observations and how to chart with online instructions with a 10-minute video. The online charting for both methods delineated the fertile window in the first 6 months. This was from day 6 until three full days past the peak day with the mucus for the CMM group and the second peak with the Clearblue Easy Fertility Monitor (i.e., the EHFM used for this study) for the EHFM group. The EHFM detects rising levels of urinary estrone-3-glucuronide (E3G), resulting in a high fertility reading on the monitor, and detects the urinary LH surge with 98.8 percent accuracy, indicating peak fertility. Mucus observations were simplified as low, high, or peak observations and low readings were considered infertile. The participants were asked to chart online daily including the days they had coitus.

In the first six menstrual cycles, with the fixed beginning of the fertile window in both groups starting on day 6, there was no difference between the two groups in the estimated fertile phase. The days of abstinence in the EHFM versus CMM groups were mean (SD) 14.34 (4.04) and 14.19 (3.86) days per cycle, respectively. After the first six cycles, the EHFM group had fewer days of abstinence with
13.25 (2.79) versus 13.68 (2.99) days per cycle in the CMM group ($t = 2.07; P = 0.039$). There was significantly more coitus in the EHFM group with 4.22 (3.16) versus 4.05 (2.88) ($t = 1.17; P = 0.026$) per cycle. The authors expressed the concern that all acts of intercourse were not being recorded as this was fewer than have been recorded in other studies.

**Comments:** This study is significant in that it is the first to analyze days of abstinence and frequency of coitus in two simple online programs of NFP, comparing a mucus only program versus an EHFM program. It appears that the EHFM may more confidently identify the fertile window, thus allowing more coitus on days of infertility for those wishing to avoid pregnancy. It is also significant in that it is an analysis of an online program with an online charting system. There are programs that train couples online or have aspects of charting online, but their effectiveness has not been formally studied. Fehring and Schneider (2014) and their fellow researchers have made simple online programs available to anyone in the world, if they have a computer and Internet access, making the living out of the Church's teaching on family planning easier to attain.

**Source**


**Recent Data on the Odds of Divorce with Contraception**

Reviewed by Patrick Herrick, M.D., Ph.D.

The Austrian Institute of Natural Conception Regulation (INER) has published a new study, which increases the available information about the risk of divorce associated with use of contraception (Rhomberg, Rhomberg, and Weissenbach 2013). Researchers from the Austrian Institute surveyed 1,131 German-speaking member couples of this sympto-thermal natural family planning (NFP) organization; 491 couples returned the survey, yielding a 43 percent response rate. The Austrian Institute of Natural Conception Regulation reported among all
respondents a 3.1 percent (25 of 811 individuals) divorce rate. Rhomberg et al. (2013) also performed some additional retrospective analysis of the divorced in their sample, regarding their ever having used contraception. They found that 77 percent of the divorced had used contraception at some time within marriage, as opposed to 40 percent in the entire survey sample.

The authors made some interesting observations, with respect to separating the effects of religion and family planning method. Twenty percent of the respondents were Protestant; the authors stated they found no association of divorce with denomination. Moreover, subgroup analysis controlling for religiosity (not denomination) showed a low divorce rate of 12.5 percent even for those NFP members in the lowest tertile of religious practice. This subgroup did not regularly participate in Church services, individual or spousal prayer. From this finding, the authors stated that “the question arises whether the practice of SymptoThermal Method (STM) per se could be a factor that contributes to the stability of marriages,” i.e. whether avoidance of contraception improves marital stability, independent of the (admitted) influence of religiosity.

Comments: The divorce rate of NFP users in this study is apparently quite low (3.1%) as compared with the general population, but the authors did not attempt any statistical test of that hypothesis. Moreover, the authors report that those who were divorced in their sample had an apparently higher rate of contraceptive usage (77%, as opposed to 40% in all respondents) at some point within marriage, but did not perform any statistical test upon that figure, either. This reported differential rate of contraception raises the question of a “dose-response gradient” for contraception and divorce; i.e. though INER members apparently get divorced less than the general population, those who had adhered to NFP most faithfully had the lowest divorce rate.

There are some questions about sampling in this report. Though the authors did apparently survey all active members of INER, it is not clear if they attempted to survey all former members. They did report contacting at least some members “no longer tightly connected” to INER. If they did contact all former members, this would represent the entire population of INER, and thereby render moot the question of
random sampling; leaving only the question of whether INER is representative of other NFP user populations. It seems reasonable that it would be, at least of NFP groups in Western developed nations. Although the authors state that the survey response rate was “within the expected range,” 43 percent is low, raising the possibility of non-response bias.

The authors did not control for other possible confounding effects, such as age, educational level, employment, and financial stability. They did report some baseline characteristics of their survey sample. That 40 percent of respondents were university educated, raises the question of whether socio-economic status influenced their findings. However, one would expect to find a higher divorce rate than 3 percent in the college-educated, so it would appear that socio-economic status cannot entirely explain their results.

The INER survey was collected at a single point in time (late 2008), but it measured events occurring over many years (up to 37 years of recorded cycles, and up to 50 years of marriage), making it a pseudo-longitudinal study; that it enrolled respondents by input variable (NFP instruction) and not output variable (divorce) makes it a pseudo-prospective study (Bailar et al. 1984). Questionnaires of past exposure are subject to recall bias, but the distinctive nature of practicing NFP, and especially of divorce, are things that individuals are unlikely to forget. A questionnaire also does not afford the same strength of inference, as a study in which input variable has been validated. In a study of contraception, such validation could take the form of pill counts, or urine hormonal measurement. Such validation was not done in the Rhomberg et al. (2013) study.

The Rhomberg et al. (2013) study has the benefit of a large sample size, an attempt to measure an entire population of NFP users (the INER population), as well as the fact that it is a relatively recent investigation. It found a remarkably low rate of divorce among current and former NFP users. The Rhomberg et al. study's main limitation was a low survey response rate, but, combined with clinical judgment, the response rate was not so low to preclude inferring a salutatory effect of NFP upon marital stability. Considering the hierarchy of evidence, pseudo-longitudinal studies are low quality, but given the dearth of other studies upon this question, at the present, it is
reasonable for physicians to tell their patients that recent evidence shows contraception usage is associated with a higher rate of divorce. There have been other studies, of varying quality, regarding the effects of contraception upon marital stability. Due to the seriousness of divorce and its effects upon health and families, physicians, and others who are called upon to advise the public, would benefit from a review of all available studies upon this question.

Sources


Acknowledgements

The author wishes to thank Joshua Mammen, M.D., Ph.D., Michael Caughron, M.D., Anna Herrick, and Austin Welsh, M.D., for their critical reviews of the original manuscript; as well as the Catholic Social Science Review for their gracious permission to use data from the Rhomberg et al. (2013) study.

Biography

• Richard J. Fehring is professor emeritus, Marquette University College of Nursing, Milwaukee, Wisconsin, USA. His email address is richard.fehring@marquette.edu.